IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

OSTERHOFF et al.

Atty. Ref.: **35-196**

Serial No. **09/731,657**

Group: **1646**

Filed: **March 12, 2001**

Examiner: **Ulm**

For: **EPIDIDYMIS-SPECIFIC RECEPTOR PROTEIN**

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December 23, 2002

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

RESPONSE

Responsive to the Official Action dated June 21, 2002, entry and consideration of the following remarks and the attached are requested; the period for response having been extended up to and including Monday, December 23, 2002, by submission of the requisite petition and fee, attached.

Reconsideration is requested.

Claims 1-30 are pending. Claims 6-16, 18-20 and 23-30 have been withdrawn from consideration. Claims 1-5, 17, 21 and 22 are under active consideration.

Attached is a copy of the pending claims of the applicants' co-pending application Serial No. 09/629,437, as well as an Information Disclosure Statement and PTO 1449 Form listing the attached Chuntharapai (Generation of Monoclonal Antibodies to Chemokine Receptors (1997) METHODS IN ENZYMOLOGY 288:15-27), cited by the present Examiner in the co-pending application. Also attached and listed on the attached PTO 1449 Form is a copy of Chen et al (Molecular Pharmacology (2000)

57:125-134) and Chen et al (J. Pharmacol Toxicol (1999) 42: 199-206) which are being submitted for the reasons described below. Consideration of the attached, along with the attached copy of the Declaration of Dr. Ulrich Gottwald, the original of which was submitted in the co-pending application, and return of an initialed copy of the attached PTO 1449 Form, pursuant to MPEP § 609, are requested.

The Section 101 and Section 112 rejections of claims 1 to 5, 17, 21 and 22, are traversed. The pending claims define patentable subject matter and are supported by an enabling disclosure. Consideration of the following in this regard is requested.

The Examiner's reliance on Brenner v. Manson 148 USPQ 689 (S Ct 1966) is misplaced as the Patent Office has previously acknowledged that Brenner dealt with the rare situation where "an applicant fails entirely to indicate why the claimed invention is useful." See, fn, 4, page 16 of "Legal Analysis Supporting Utility Examination Guidelines", Department of Commerce, Patent and Trademark Office, Docket No. 950706162-5172-01 executed July 3, 1995, by Bruce A. Lehman, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks (copy attached). The Patent Office has recognized that Brenner required an applicant to disclose a utility in his application. Specifically, the Patent Office has noted that:

> "Courts have found an application deficient under the "usefulness" portion of § 101 where the applicant has not identified [emphasis added] any "specific" utility for the invention. Such situations arise rarely; namely where an applicant fails entirely to indicate why the claimed invention is useful. For example, in Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966), the Supreme Court affirmed a finding by the Office that a method of producing a particular class of steroids was deficient under § 101 because the applicant did not

explain why the compounds produced by the claimed process were useful. The process in question was patented by another who had disclosed a utility for the invention. The Court refused to consider sufficient a general assertion, not made in the application as filed but instead made by the applicant during an interference proceeding, that the compounds in question were structurally similar to others and therefore might possess a particular biological activity in common with those other compounds. Thus, the Court focused on the fact that the applicant failed to identify any "specific utility" for the claimed invention in his application. A more recent case involved an assertion that a disclosure that a substance was "plastic-like" and could be pressed into films was insufficient to satisfy § 101. In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). As the court stated:

> Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility. Ziegler did not even assert that the polypropylene was useful in applications where any of the solid plastics were used. Rather, Ziegler said the polypropylene was "plastic-like."

Id. at 1203, 26 USPQ2d at 1605. Thus, the failure of the applicant to either identify any use for the invention or to disclose features of the invention that would make uses of it readily apparent, was found to render the claimed invention deficient under § 101." Id.

Moreover, the Patent Office has appreciated that

> "Practical considerations require the Office to rely on the inventor's understanding of his or her invention in determining whether and in what regard an invention is believed to be "useful"...
> Courts have repeatedly found that the mere identification [emphasis added] of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to

the public" and thus satisfies the utility requirement. As the CCPA held in Nelson v. Bowler:

> Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility. [206 USPQ at 883.]

Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. Accordingly, Office personal should not construe § 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans.

These general principles are equally applicable to situations where an applicant has claimed a process for treating a human or animal disorder. In such cases, the asserted utility is usually clear--the invention is asserted to be useful in treating the particular disorder. If the asserted utility is credible, there is no basis to challenge such a claim on the basis that it lacks utility under § 101." [Footnote references omitted.] Id, at pp. 4-5.

The footnotes of the Patent Office's Legal Analysis are instructive in providing a summary of the courts' requirements and are reproduced in the following for the Examiner convenience.

"[23] The utility being asserted in Nelson related to the a compound with "pharmacological" utility. Nelson, 626 F.2d at 856, 206 USPQ at 883. Office personal should rely on Nelson and other cased as providing general guidance when evaluating the utility of an invention that is based on any therapeutic, prophylactic, or pharmacological activities of that invention.

In Nelson v. Bowler, the CCPA addressed the practical utility requirement in the context of an interference proceeding. Bowler challenged the patentability of the invention claimed by Nelson on the basis that Nelson had failed to sufficiently and persuasively disclose in his application a practical utility for the invention. Nelson had developed and claimed a class of synthetic prostaglandins modeled on naturally occurring prostaglandins. Naturally occurring prostaglandins are bioactive compounds that, at the time of Nelson's application, had a recognized value in pharmacology (e.g., the stimulation of uterine smooth muscle which resulted in labor induction or abortion, the ability to raise or lower blood pressure, etc.). To support the utility he identified in his disclosure, Nelson included in his application the results of tests demonstrating the bioactivity of his new substituted prostaglandins relative to the bioactivity of naturally occurring protaglandins. The Court concluded that Nelson had satisfied the practical utility requirement in identifying the synthetic prostaglandins as pharmacologically active compounds. In reaching this conclusion, the court considered and rejected arguments advanced by Bowler that attacked the evidentiary basis for Nelson's assertions that the compounds were pharmacologically active.

In In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980), an inventor claimed protection for pharmaceutical compounds for treating leukemia. The active ingredient in the compositions was a structural analog to a known anti-cancer agent. The applicant provided evidence showing that the claimed analogs had the same general pharmaceutical activity as the known anti-cancer agents. The Court reversed the Board's finding that the asserted pharmaceutical utility

> was "incredible," pointing to the evidence that showed the relevant pharmacological activity.
>
> In Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), the Federal Circuit affirmed a finding by the Board of Patent Appeals and Interferences that a pharmacological utility had been disclosed in the application of one party to an interference proceeding. The invention that was the subject of the interference count was a chemical compound used for treating blood disorders. Cross had challenged the evidence in Iizuka's specification that supported the claimed utility. However, the Federal Circuit relied extensively on Nelson v. Bowler in finding that Iizuka's application had sufficiently disclosed a pharmacological utility for the compounds. It distinguished the case from cases where only a generalized "nebulous" expression, such as "biological properties," had been disclosed in a specification. Such statements, the court held, "convey little explicit indication regarding the utility of a compound," 753 F.2d at 1048, 224 USPQ 745 (citing In re Kirk, 376, F.2d 936, 941, 153 USPQ 48, 52 (CCPA 1967))."

The applicants note that the present application describes a number of useful products of the disclosed invention, as required by the courts. The comments noted by the Examiner in the applicants' publication (DNA and Cell Biol 16(4) 379-389 Apr 1997) are not evidence of a lack of a disclosed utility of the present application. The Examiner must appreciate that the cited publication discloses a utility while appreciating that further work, such as a reasonable amount of experimentation, may always be required or even "essential." Moreover, the Examiner's reference to passages in the applicants' journal article fail to enlighten the analysis of the present disclosure, which describes a number of practical utilities for the disclosed and claimed invention.

The applicants note, for example, that one of ordinary skill has appreciated that nucleotide sequences which code for polypeptides of the human epididymis, the corresponding expression products, and antibodies directed against them, are useful for diagnosis and treatment of male infertility. See, page 4, lines 4-9 of the present specification, which discusses EP-A-0440 321.

Similarly, the present application identifies substantial and specific utilities of the presently claimed invention, i.e., methods and treatment of male infertility, such as when caused by protein metabolism disturbances in the epididymis, and compounds and compositions to perform these methods. See, for example, page 4, lines 12-15; page 12, lines 20-25; page 13, lines 3-4; page 13, lines 6-18; page 14, lines 11-14; page 14, lines 22-26; page 14, lines 28 to page 15, line 7; and page 17, lines 7-9 of the specification.

Accordingly, the Examiner's statements on page 4, of the Office Action dated June 21, 2002 (Paper No. 11) that "the instant specification does not identify any disease or disorder which can be diagnosed by the detection of the presence or absence of this protein or which can be treated by the addition or removal of this protein" is incorrect.

The Examiner appears to believe that the identification of a tissue-specific marker is not a specific or substantial utility worthy of patent protection. The applicants note however that this assertion is contrary to the CCPA's statements in Nelson, quoted above with approval by the Commissioner of Patents. That is, the new detection capability provided by such tissue-specific reagents which are related to the disorder of

male infertility, provides the medical profession with the opportunity to more quickly combat illness and/or alleviate symptoms of such a disorder. Moreover, the applicants note that the present specification identifies more than such a diagnostic utility, as described above.

As a demonstration of the utility of the presently disclosed invention, the applicants have performed, or had performed, the following experiments.

The experiments described in the attached Declaration were performed to demonstrate a utility of a receptor protein designated HE6, and of antibodies against this protein. The receptor protein HE6 has the amino acid sequence shown in SEQ ID NO:2 of the present application.

The attached Declaration of Dr. Gottwald clearly demonstrates that the protein referred to as HE-6 in the present application is a protein with biological significance (contrary to the objection raised by the Examiner; on, for example, page 6 Paper No. 11). Specifically, the Declaration demonstrates that knocking out the HE-6 gene results in infertility of mice. One of ordinary skill in the art will appreciate from the attached and the present specification that the claimed invention, as represented by HE-6, is biologically significant and useful and that the utility is a result of the biological effects or significance.

Since HE-6 at least contributes to fertility of mice, the protein can be used to screen for substances suitable for male contraception. Contrary to the conclusion of the Examiner screening for agonists can be carried out even if the natural ligand of a protein is unknown. This is shown for example for G-protein linked receptors (see

publications of Chen et al., attached). As is clearly stated in the introduction of these publications the effect of overexpression of the receptors was already known prior to 1998.

Based on the knowledge of the present application (sequence of the HE-6 DNA and protein) and the common generally advanced knowledge of one of ordinary skill in the art, one of ordinary skill in the art would have been capable of, for example, producing an overexpressing cell and using it for screening for agonists.

Further, the protein of the above application can be used for diagnosis of infertility of humans. Since absence of HE-6 results in infertility, the protein is useful for identification of infertility based on expression of HE-6 or the absence thereof. A respective test could, for example, immunologically detect HE-6 on sperm cells. An example of a respective detection assay is enclosed as a summary of experiments generated by the present applicant (presentation titled "HE-6 expression on sperm surfaces spermatozoa collected from caudal epididymis").

In view of the above and attached, the applicants submit that the claims define patentable subject matter which is supported by an enabling disclosure.

The Section 112, second paragraph rejection of claims 1-3, 5 and 17 is traversed. The applicants submit the "derivatives"' of the present claims are sufficiently described by the present disclosure, as noted by the present Examiner in an Office Action dated July 18, 2001 issued in the co-pending application Serial No. 09/629,437 (Paper No. 5). See, page 7, lines 10-15 of Paper No. 5 issued in the co-pending application. The Examiner's objections of claims 2, 3 and 5 relating to alternative claim

recitations is not understood, especially in view of the lack of a similar rejection of claim 1, and clarification is requested in the event the rejection is maintained.

The claims are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection of claims 1-3, 5 and 17 is requested.

The Section 102 rejection of claim 1-5, 17, 21 and 22 over Osterhoff is traversed.

Osterhoff et al. is the applicants' own publication, which was published April 1997, i.e., within a year prior to the filing of the parent application (Serial No. 09/041,745, filed March 13, 1998). The applicants submit that the parent application provides an enabling disclosure of the presently claimed invention and provides an adequate written description of the presently claimed invention. The applicants submit that the parent, like the present application, meets the requirements of Section 112, first paragraph, such that benefit of the parent application should be afforded, along with withdrawal of the Section 102 rejection.

In view of the above and attached, the claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

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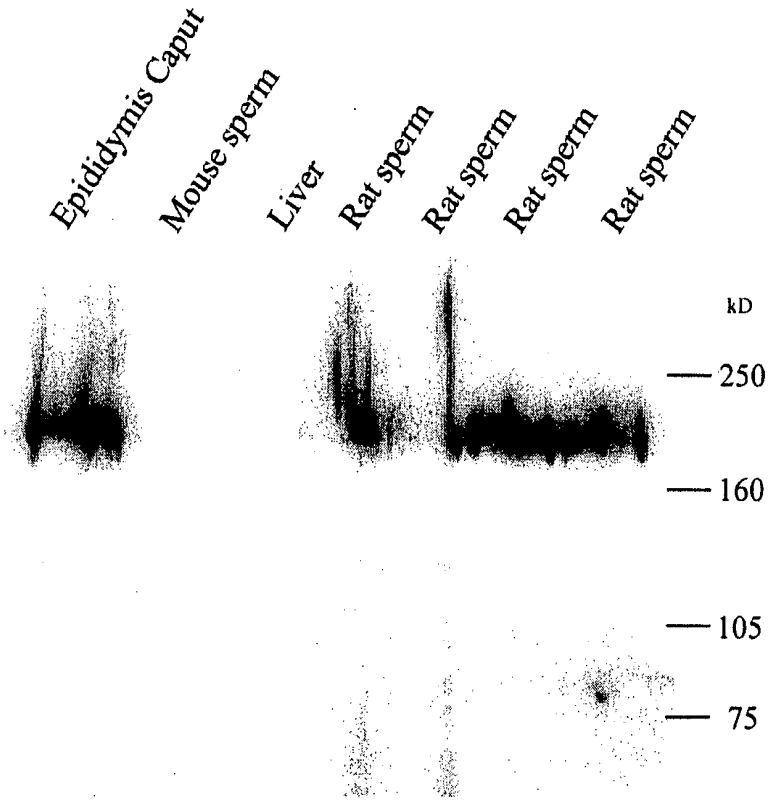
HE6 expression on sperm surfaces
Spermatozoa collected from caudal epididymis



Spermatozoa collected in buffer with protease inhibitors
Protein denaturation before loading: 45°C, 5 min.
First antibody used: mN2 (animal 1, day 90); Antibody dilution: 1:2500
Second antibody anti rabbit; dilution: 1:3000 (ECL Western detection system)

Data generated by Schering AG, 2002